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HEALTH EFFECTS OF SLEEP DEPRIVATION



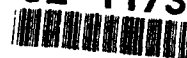
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13. ABSTRACT (Maximum 200 words) Biomedical and health consequences of total, selective, and partial sleep loss were documented in this paper by examining adrenomedullary activity, adrenocortical activity, metabolism, hematological and immunological changes, autonomic nervous system activity, epileptiform discharges, physical work capacity, antidepressant effects, and mental health.				
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HEALTH EFFECTS OF SLEEP DEPRIVATION

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Early to bed and early to rise, makes a man
healthy, wealthy and wise.

Poor Richard's Almanac

Effects of sleep loss on job performance
are well documented in many review papers
and a recently published monograph.¹¹⁸ In con-
trast, health consequences of acute and chronic
sleep loss have been poorly documented except
in a few social and epidemiological surveys on
shift- and nightwork. The purpose of this chapter
is to survey and critically review the results of
laboratory and field studies on health conse-
quences of sleep loss. Three kinds of sleep loss
are identified: total, selective, and partial sleep
loss. The most critical information for practi-
tioners of occupational medicine is the health
consequences of loss of several hours of sleep
repeatedly every day over many days or months—
that is, chronic partial sleep deprivation. Unfor-
tunately, this survey found that very few chronic
partial sleep loss studies were conducted owing
to the prohibitive cost of running them and,
more importantly, to the apparently minimal
health effects of sleep loss. This paper describes
and evaluates the currently available data base
to determine the effects of different kinds of
sleep loss on the functional integrity of the
human organism. The factors discussed include:
adrenomedullary activity, adrenocortical activ-
ity, metabolism, hematological and immuno-
logical changes, autonomic nervous system
activity, epilepsy, physical working capacity,
antidepressant effects, and mental health.

BACKGROUND

It is commonly believed that we need approximately 7-8 hours of sleep every night and that sleep serves a restorative function. Some people think that missing this period of restoration of mind and body may present an immediate threat to health, or that chronic sleep deprivation may shorten life span or increase morbidity. When we stay awake all night, our body misses the surge of putatively restorative human growth hormone (hGH) that occurs during nocturnal sleep and, at the same time, gets an overabundance of "stressor substance," such as norepinephrine and corticosteroids.

However, everybody has experienced going without sleep at one time or another, either totally for one or two nights, or for a few hours nightly over several days. Many ordinary life events, such as working to meet deadlines, earning a living as a night- or shiftworker, or managing family and business emergencies, can lead to temporary total or partial sleep deprivation. Can such a common life experience be dangerous or fatal?

A series of reports on sleep deprivation studies in rats by Rechtschaffen and his group^{25,26,33-35,91,152,153,239,240} suggests that it might. Rats subjected to total sleep deprivation or to selective rapid eye movement (REM) sleep deprivation died in approximately three or five weeks, respectively. Rechtschaffen and others²⁴⁰ speculated on the basis of energy requirements that humans would "survive sleep loss about 3.7 times longer than rats, or about 77 days of total sleep deprivation versus 21 days of rats, and 135 days of partial sleep deprivation versus 37 days of rats" (p. 80). Horne¹¹⁸ raises serious doubts about generalizing the findings in rats to humans. The rat's small body requires much more constant effort, or larger energy expenditures, to maintain core body temperature than the much larger human body with its more adequate thermoregulatory mechanisms. Death in severely sleep-deprived rats might be due more to thermoregulatory failure, which would not be expected to occur in humans, than to sleep loss itself.

During World War II, greater London over a six-year period experienced frequent air raids with nightly disruptions of sleep, but Pai²¹⁸ reported no ill effects of sleep loss among a large number of people. Progressively increasing sleepiness serves as a built-in safety valve that works to prevent accumulation of an inordinate sleep loss (as hunger and thirst prevent us from going too long without food and water). Because of this, it takes great personal effort or vigorous social support to remain awake for more than 48 hours.

Our impression is that direct detrimental health consequences of sleep loss are probably minimal.^{107,128,141-143} The reports of healthy insomniacs who need little or no sleep^{128,180,181} seem to support this view. Nonetheless, it is possible that sleep loss interacts with stressful environments or biological weaknesses to the detriment of health. This might explain the cases of "sleep loss psychosis" reported in early literature.^{43,319} In what follows we will summarize research findings on the health consequences of sleep loss and attempt to separate fact from myth in this somewhat controversial area.

The purpose of this report is to provide medical professionals who are responsible for maintaining the health of men and women in shift and irregular work environments with background information on the medical consequences of sleep loss. There is an increasing need for such knowledge because more and more military and civilian personnel are involved in shiftwork and round-the-clock sustained/continuous operation (SUSOP/CONOP). The increase in SUSOP/CONOP in the military is documented in a technical report by U.S.

Army Combined Arms Combat Development Activity on "Continuous Operations Study (CONOPS) Final Report," published in 1987 and available to U.S. Government Agencies (AD-B111424L). We will not here discuss the effects of partial and total sleep deprivation on psychomotor and cognitive tasks, because many readily available reviews^{118,170,188,192,198,200,204,325,327} have been produced since the publication of the *Handbook of Human Engineering Data* in 1952 by Tufts College.

Before we discuss biomedical effects of sleep loss, we need to define what we mean by sleep deprivation. Researchers have, so far, recognized three kinds of sleep deprivation:

- (1) Total sleep deprivation
- (2) Partial sleep deprivation
- (3) Selective sleep deprivation.

Total sleep deprivation means getting no sleep during at least one 24-hour cycle. For example, if a person who usually sleeps from 2300 to 0700 awakens one morning at 0700 and stays awake until 2300 of the following day, that person has gone 40 hours without sleep. During this 40-hour period, one 8-hour sleep period has been missed. Strictly speaking, 8 hours of total sleep deprivation have occurred. However, in general practice, we use the hours of continuous wakefulness—40 hours in this example—as the amount of total sleep deprivation.^{197,200}

We frequently experience **partial sleep deprivation**. Partial sleep deprivation means sleeping less than usual.^{198,274,316,325,326} In research, partial sleep deprivation has been created in two ways: (1) a gradual reduction in sleep duration; for example, a reduction by 30 minutes every two weeks, providing sleepers with an ample opportunity to adjust to longer waking hours each day,^{100,125} or (2) a sudden reduction in sleep duration, for example, from a customary 8 hours to 5. The short sleep regimen is tried out for a few days^{57,108,111,120,209,273} or continued for a long period of time so that sleepers can adapt to the new life-style.^{100,315,325}

Unlike total and partial sleep deprivation, clear-cut **selective sleep deprivation** does not occur in real world situations. It is created only as a result of manipulation of sleep in a laboratory, where changes in sleep stages can be observed as they take place. When sleep is observed electrophysiologically, it is classified into seven states: wake; sleep stages 1, 2, 3, 4; REM sleep; and movement time. Often, sleep stages 3 and 4 are combined and designated as slow wave sleep (SWS), which is contrasted to the amount of REM sleep. Sleep stage 1 is thought to be a transition stage, when we are neither asleep nor awake.¹³¹ Sleep stage 2 has a unique brain wave signature, "sleep spindles," indicating that at this stage we are fully asleep. Although the functions of sleep and the various sleep stages are not fully understood,^{40,116-118} it has been suggested that SWS is needed for "body repair," whereas REM sleep is needed for "mind repair."^{77-80,88,217,302} In nocturnal sleep of adults with no sleep disorders, these sleep stages follow each other in a fairly fixed pattern, creating a fairly predictable sleep profile. (For a more complete discussion of the sleep stages, see Rechtschaffen and Kales.²⁴¹)

Selective sleep deprivation consists of preventing the occurrence of a particular sleep stage. In REM sleep (or SWS) stage deprivation, sleepers are prevented from getting REM sleep (or SWS) by being awakened whenever they begin to enter that sleep stage.^{5,13,77,305}

The sleep deprivation we experience in daily life is likely to be a mixture of these three types. For example, we may simultaneously experience both partial and REM sleep deprivation when we curtail our sleep by waking up a couple of

hours earlier in the morning, thus missing the early morning sleep that is rich in REM sleep. Taking antidepressants or hypnotics has also been shown to reduce REM or SWS.^{12,132,217} In this report, we are mostly concerned with health effects of total sleep deprivation, because that is what the majority of the research has dealt with.

SLEEP LOSS AND ADRENOMEDULLARY ACTIVITY

The adrenomedullary system produces two separate catecholamines, epinephrine (EP) and, in small quantities, norepinephrine (NE). These hormonal secretions are rapidly increased by stressors such as cold, pain, anoxia, shock, hypoglycemia, hypotension, physical exercise, psychological stimuli, and drugs in common use, such as caffeine, nicotine, and alcohol. Both EP and NE act on all organs of the body, causing "sympathetic activation," a collection of effects generally serving to improve physical effectiveness for "fight or flight" emergency situations.^{116,118} These effects include increased heart rate, strengthened cardiac contraction, constriction of arterioles in the skin, and both vasodilation and constriction of voluntary muscle arterioles. NE is generally more powerful in raising blood pressure, while EP is generally more powerful in the mobilization of glucose and fat and the relaxation of smooth muscles. Urinary EP shows a strong circadian rhythm, but urinary NE shows no significant circadian rhythm.^{9,102,103,110,116} Thus any changes in EP during sleep deprivation must be analyzed to partition out the circadian component.

Fiorica et al. observed no significant changes in total urinary catecholamines during 85 hours of total sleep deprivation.⁹⁵ Levi^{158,159} also found no consistent changes in EP or NE up to 75 hours of total sleep deprivation, when he did not take experimental subjects' age into account. No significant increase in 24-hour urinary EP was seen in his older subjects (49–64 years, average age 56). However, 24-hour urinary EP increased in the young group (20–44 years, average age of 29). Levi attributed the results to differences observed in self-pacing between the young and old. Early in the experiment, the young subjects mobilized more physical and mental resources to achieve superior performance, but subsequently they slackened their work pace owing to exhaustion. The old subjects seemed more in control of and less reactive to the study environment and kept a more even pace throughout the experiment. Froberg found that "morning-type" people did not differ from "evening-type" people in circadian rhythms of urinary EP secretion during 72 hours of total sleep deprivation. Sleep loss neither disrupted circadian rhythm nor increased urinary EP excretion. Excretion of vanillylmandelic acid, a major metabolite of NE, did not change during a total of 205 hours of sleep deprivation.¹⁰²

From these studies we could conclude, as previous review papers have,^{110,116,199} that no consistent significant increase in the adrenomedullary activity occurs during total sleep deprivation. In other words, total sleep deprivation in itself does not cause "stress" in the usual sense.

Some studies, however, have suggested an adrenomedullary activation during total sleep deprivation. Steinberg and others²⁷⁹ studied the effects of total sleep deprivation, sleep, and immobility on the levels of EP, NE, metanephrine, normetanephrine, and vanillylmandelic acid under a strictly controlled diet. They found higher urinary catecholamine excretion during nights of sleep deprivation when subjects lay on a bed (but remained awake) than during nights of normal sleep. Other urinary substances showed no change. They concluded that wakefulness caused significant elevation in EP and NE. Kuhn and his group performed a

series of studies¹⁴⁸ examining the effects of 5 days of total sleep deprivation on 24-hour urine levels of metanephrine, normetanephrine, and vanillylmandelic acid. They observed a significant increase of normetanephrine during sleep deprivation days (except day 2), a significant increase in metanephrine on day 3, and a significant increase in vanillylmandelic acid on the last day of the study. These responses were interpreted as reflecting stress caused by enforced sleep loss of 5 days. However, Kuhn et al. imposed greater psychological and physical demands and other situational factors on their subjects than the previously discussed studies. These stressors, rather than the sleep loss itself, may have caused the adrenomedullary activation.

Hasselman et al.¹¹² reported higher urinary EP and NE during bicycle ergonomic work after one night of sleep loss than after a normal night's sleep. It appears that sleep-deprived subjects may be able to perform the same amount of physical work as usual, but in doing so, they must increase adrenomedullary activity for greater mobilization of energy resources. They also found that ambient temperature is an important situational factor affecting adrenomedullary output. They observed a dramatic increase of urinary catecholamines when the sleep-deprived subjects worked with a bicycle ergometer under high ambient temperature. Thus, sleep deprivation appears to interact with other stressors rather than directly affecting adrenomedullary activation.

In summary, total sleep loss of 3 days or less causes neither significant increases in adrenomedullary activity nor circadian disruption of EP rhythm if sleep deprivation is conducted under physically and mentally nondemanding, experimental environments. When total sleep deprivation takes place in high physical and mental workloads under uncomfortable ambient temperature, or the subjects are particularly energetic in their efforts to maintain top performance by adopting a high work pace, a significant activation of the adrenomedullary system may be reflected in increased urinary catecholamines.

SLEEP LOSS AND ADRENOCORTICAL ACTIVITY

The pituitary-adrenocortical system produces glucocorticoids, mineralocorticoids, and androgenic steroids. The main glucocorticoid is cortisol. Production of cortisol increases in response to many stressors—for example, surgery or illness. Cortisol increases hepatic glycogenesis, suppresses protein synthesis, and has anti-insulin action in peripheral tissues, thus providing energy needed for coping with prolonged, stressful circumstances. The cortisol level sensitively reflects psychological states, increasing with arousal and anticipation of stress.

Because of difficulties in assaying serum cortisol, early studies used the quantity of eosinophils, lymphocytes, and urinary 17-ketosteroids and electrolytes (factors affected by adrenal steroids) to indirectly monitor activation of the pituitary-adrenocortical system. Attempts to determine whether total sleep deprivation would activate the pituitary-adrenocortical system were further complicated by the presence of a strong circadian rhythm in these hormones.

Urinary 17-ketosteroids have been found to show no change after 72 hours of total sleep deprivation⁴³ and were even reported to decrease on the second, third, and fourth days of total sleep deprivation.^{190,293,324} Urinary 17-hydroxycorticosteroids were also observed to show no change after 72 or 120 hours of total sleep deprivation,^{43,143} and one night of total sleep deprivation did not change the time of the circadian peak of plasma 17-hydroxycorticoid.⁹⁸ Rubin et al.²⁵² found that plasma and urinary 17-hydroxycorticosteroid decreased from the baseline

value to a low point after 170 hours of total sleep deprivation. These differences in results probably reflect more the varied psychological and physical demands imposed on the subjects than the effects of sleep loss itself.^{191,198} Opstad and Aakvaag²⁰⁹ observed levels of serum cortisol during 5-day-long training field exercises. These training courses required heavy and continuous physical activities with less than a total of 2 hours of sleep per 24 hours. Serum cortisol decreased from a relatively high level on day 1 to a low level on day 5. Similarly, a reduced cortisol level was observed at the end of 48 hours of sleep deprivation among subjects who did not experience heavy physical work. Kant et al. observed slight decreases in urinary cortisol levels during sleep loss of 72 hours.¹³²

In contrast, Kuhn et al.¹⁴⁸ reported an increase of urinary 17-hydroxycorticosteroid for the first two days of total sleep deprivation.

Briefly, total sleep deprivation of up to 72 hours has little effect on glucocorticoids, especially compared with the large increases in 17-hydroxycorticoid sometimes observed during baseline periods when subjects are experiencing pre-experiment excitement and anxiety. Total sleep loss does not cause the classical nonspecific emergency reaction.

SLEEP LOSS AND METABOLISM

People expend more metabolic energy during a sleepless day than during a normal 24-hour cycle. The metabolism slows down during sleep, and this energy conservation does not occur during sleep deprivation.

Biological energy is based on the adenosine triphosphate (ATP) system. Thus, total sleep loss might be anticipated to affect ATP. Luby et al. reported that after 4 days of sleep deprivation energy production (as measured by specific activity of ATP after whole blood was incubated with radioactive phosphorus) increased, while the ATP level dropped.¹⁶⁶ After 7 days of total sleep deprivation (TSD), energy production had dropped almost to baseline, whereas the level of ATP had risen but was still below baseline. Unfortunately, this study involved only one subject and has never been replicated.

When the ATP reserve is depleted, phosphocreatine is used as a high energy source. Under these conditions the level of urinary creatinine may indirectly signal the degree of energy expenditure. However, a number of studies have found that total sleep deprivation of up to 120 hours does not change the urinary creatinine level.^{95,143,270} Resting metabolism as assessed by oxygen consumption also remain unchanged during total sleep deprivation of up to 120 hours.⁹⁵

If total sleep deprivation is a catabolic state, it might cause an acceleration of protein turnover, which should be reflected by an increase in the urinary total nitrogen. However, total sleep deprivation of up to 126 hours did not affect the 24-hour urinary total nitrogen level.¹⁴⁸ Scrimshaw et al.²⁷⁰ observed a decrease of urinary nitrogen on the first day of total sleep deprivation and an estimated 12% increase in protein requirement over the basal need during the second day. Kant et al.¹³² found an increased urea excretion within 24–48 hours of sleep deprivation, and it stayed high during the remainder of a 72-hour sleep deprivation. This finding was interpreted to reflect the increased protein catabolism to supply energy needs. Adam and Oswald, studying rats' brains, found less protein synthesis during 13 hours of total sleep loss but increased protein synthesis during the subsequent recovery sleep.

Under some circumstances, where sustained physical activities are required, the body may convert from carbohydrates to lipids as the primary fuel for

biological energy. It appears that total sleep deprivation in environments requiring constant mental alertness and physical activity falls in this category.^{249,250} The research findings of Kuhn et al.^{110,148} indicate that lipids are a preferred energy source during total sleep deprivation. They found that plasma-free fatty acids increased by 130% and 182% after 48 hours and 72 hours of total sleep deprivation respectively. They detected a much slower fall in the blood glucose level after glucose ingestion after sleep loss than before; after 3-4 days of total sleep loss, a "glucose tolerance curve" resembled the curve for borderline diabetics. Vondra et al. found that hyperglycemia in response to an oral glucose tolerance test was prolonged after 120 hours of sleep deprivation.³¹¹ This result was accompanied by a decreased input of pyruvate into the Krebs cycle. Van Helder et al.²⁹⁷ believe that this change in glucose metabolism is a prediabetic type of metabolic state. They found that subjects who were deprived of sleep for 60 hours and physically exercised developed insulin resistance. Their proposal that sleep loss results in decreased insulin sensitivity at peripheral insulin receptor sites, eventually leading to "insulin exhaustion at pancreatic sites," needs confirmation because the receptive role played by physical exercise was not clearly separated from the role of sleep loss in itself. Unlike Kuhn et al.¹⁴⁸ and Vondra et al.,³¹¹ they observed no protracted glycemia, possibly because of the relatively short (60 hours) sleep deprivation against that of 120 hours. Fiorica et al.⁹⁵ showed that the respiratory quotient also reflected a shift from carbohydrate- to lipid-dominated metabolism on the second and third days of total sleep deprivation.

Total cholesterol in plasma and in the vastus lateralis muscle and plasma triglycerides decreased during a 120-hour sleep deprivation.³¹¹ The changes resembled alterations in cholesterol metabolism observed in cardiovascular diseases or the conditions preceding them.

Sleep deprivation was reported to increase plasma levels of thyroid (T_3 , T_4 , and rT_3) hormone,^{214,220} increasing metabolic rate. Opstad and Aakvaag²¹¹ found that the combined effect of sleep deprivation, prolonged heavy physical work, and caloric deficiency caused thyroxine to increase on day 1 but to decrease from day 2 to day 5, the end of the training course. Triiodothyronine showed a similar trend to T_4 . Palmblad et al.²²⁰ found very small increases of about 10% for T_3 and T_4 plasma levels after 48 hours of sleep deprivation.

Sleep loss reduces androgens.⁶⁸ Serum testosterone decreased during a 5-day training course involving sleep loss, hard physical work, and caloric deficiency.^{1,210,211} Testosterone decreased to below 25% of precourse levels after 48 hours of sleep loss. This decrease reflected reduced production of testosterone, not increased metabolism.

Briefly, these findings suggest that, as total sleep loss continues, skeletal muscles and other tissues begin to derive more energy from the use of free fatty acids. Total sleep loss of two nights or more may result in switching the main energy substrate from carbohydrates to lipids to meet energy demands, resulting in increased plasma-free fatty acids, increased plasma glucose, and sluggish plasma glucose use.

SLEEP LOSS AND HEMATOLOGICAL AND IMMUNOLOGICAL CHANGES

Total sleep deprivation changed neither the erythrocyte count^{98,138} nor the hematocrit level.^{95,143} However, a drop in plasma iron was reported in

humans^{147,161,300} and in rats.^{83,84} Kuhn et al.¹⁴⁸ reported that plasma iron dropped to one-half its normal level during 120 hours of total sleep loss. Their report showed that the plasma iron decline was sharp during the first 48 hours of sleep loss and subsequently much more gradual. Return to the normal value was slow, taking roughly one week. Intestinal absorption and excretion rates of iron, as measured by radioactive iron uptake, showed no changes during total sleep loss. There was no evidence of impaired erythropoiesis. Thus the reduction in plasma iron was attributed to a failure of the reclamation process of removal of iron from plasma into the splenic-hepatic reticuloendothelial system and the erythropoietic tissue in the bone marrow.¹¹⁰ Lindemann et al. used a 4- to 5-day training course involving continuous physical activities, limited caloric intake, and partial sleep deprivation (1 to 3 hours of sleep loss per night) and observed changes in hemoglobin, hematocrit, serum iron, bilirubin, and other values. Both hemoglobin and hematocrit decreased during the course. The serum iron increased until day 4 but decreased sharply to 50–60% below initial values on day 5. The bilirubin levels increased markedly, but they came down to the precourse value immediately after the training course. The elevated iron and bilirubin levels were attributed to damage to erythrocytes from the mechanical stress of heavy, continuous physical activities, and not to sleep loss itself. Similar results are reported during Japanese ranger training lasting 93 hours.³³³

The level of serum ferritin, which returns iron to the erythropoietic tissues in the bone marrow, was elevated during a 4- to 5-day training course.³⁰⁰ The increase of ferritin was correlated with decreased hemoglobin values and increased total bilirubin. Iron released from disintegrated erythrocytes increased ferritin synthesis in the reticuloendothelial system and subsequently increased release of ferritin in blood. The effects of sleep deprivation itself on erythrocytes remain unclear. Levi¹⁵⁹ reported that total sleep deprivation of 24 hours resulted in serum iron decreases of 26% in older subjects (average age, 56), while iron decreased by 52% in younger subjects (average age, 29). Erythrocyte sedimentation rate (a measure that can be affected by many things, including anemia and inflammation) of the older subjects increased by 38% and that of the younger subjects by 168%.

Drucker-Colin⁸³ and Drucker-Colin et al.⁸⁴ found that normocytic anemia can be induced in rats by administration of phenylindanedione (PID, an indirect anticoagulant) during total sleep loss. Administration of parachlorophenylalanine (PCPA, a serotonin synthesis inhibitor) along with PID during sleep loss aggravated the anemic process; anemia without evidence of PID-induced internal bleeding was detectable after 3 days of treatment. These drugs do not produce anemia when administered without accompanying sleep loss, and, as Drucker-Colin emphasized, even an 8-day-long period of sleep deprivation without the drugs does not produce anemia, indicating that sleep loss interacts with the drugs rather than acting directly to produce anemia. Earlier animal studies reported decreases in erythrocyte count, down to as low as 60% of normal.¹³⁸ The studies of Drucker-Colin et al.⁸⁴ suggest vulnerability of the hemopoietic system to combined sleep loss and drug administration.

It is common belief that the "stress" of losing sleep causes us to catch cold. Immunodeficiency may follow stressful life changes.^{118,219}

Palmblad²²¹ observed an increased production of interferon and decreased phagocytosis during 77 hours of total sleep deprivation. These changes were too small to be of clinical significance. In a subsequent study,²²² the immunological

measure of the rate of proliferation of white blood cells in response to an antigen was used. The proliferation of polymorphonuclear leukocytes and monocytes after antigen exposure was reduced after total sleep deprivation of 48 hours, but it remained within normal range; the drop appears to be of no clinical significance.

Briefly, no serious immunological changes follow sleep deprivation. Reduced lymphocyte stimulability and neutrophil phagocytosis and gradually increasing interferon production are expected after 48–72 hours of sleep deprivation,²¹⁹ but these changes in cell-mediated immunity would be too small to be of clinical significance. The body's iron equilibrium may be altered during sleep deprivation, and the addition of certain drugs or other stressors may lead to anemia.

SLEEP LOSS AND AUTONOMIC ACTIVITY

Mean core body temperature gets lower during total sleep deprivation. The circadian variation remains but its amplitude is reduced. Homeostatic ability to maintain core body temperature when exposed to cold is not impaired by 84–86 hours of total sleep deprivation,⁹⁵ but Sawka et al. suggest some degraded thermoregulation during exercise after total sleep deprivation.²⁶⁰

Resting systolic and diastolic blood pressures do not change during total sleep deprivation.^{54,199} Resting heart rate has generally been found to show little systematic change during sleep loss,^{67,116,198,203,324} except Bjerner reported general systematic slowdown of resting heart rate.⁴² Fenz and Craig⁹⁴ reported that heart rate increased on day 2 of total sleep deprivation, but the increase was four \pm only in one of the two daily measures. On the third day, heart rate dropped. Total sleep deprivation caused a progressive increase in heart rate variability, much of it related to an increase in the normal tendency of the heart rate to vary with respiration—"respiratory sinus arrhythmia."¹¹⁶

Endogenously depressive patients have a lower amplitude circadian heart rate curve than normal subjects. Twenty-four hours of total sleep deprivation caused further flattening of the circadian heart rate curve in this patient group. The circadian heart rate rhythms of neurotic depressives are more normal than those of the endogenously depressive at baseline and were unaffected by a 24-hour sleep loss.²⁵³

Levi¹⁵⁸ observed that one quarter of his subjects showed S-T segment depression during 75 hours of total sleep deprivation. In some cases, depression was pronounced and resembled a cardiac infarction in the apical area. The depression gradually disappeared after several days of sleep and rest.

Johnson et al.¹²⁷ reported that resting-finger pulse volume became very small due to peripheral circulatory constriction during a prolonged total sleep deprivation. Finger pulse volume showed a marked vasodilation, tripling in volume, during recovery sleep. Mirsky and Cardon¹⁸³ observed increased finger pulse volume near the end of their total sleep deprivation study during a complex vigilance task. Such transient increases may be attributable to periods of microsleep.

Generally, total sleep deprivation does not change respiratory rate,⁹⁵ although variability of rate was reported to increase over 60 hours of sleep loss.¹¹⁶

Skin conductance probably reflects sympathetic nervous activity. Different studies have reported equivocal and conflicting results as to sleep deprivation effects on skin conductance.¹¹⁶ We conclude that total sleep loss has no consistent effect on skin conductance.²⁰³ Strausbaugh and Roessler²⁸⁰ reported that tonic

skin conductance was higher—that is, subjects were more alert and activated—in the sleep-deprived subjects who had high “ego strength” than in those whose ego strength was low.

Briefly, no major autonomic changes are expected in resting subjects during total sleep loss of 2 days or less, although amplitudes of circadian curves may be blunted and general variability may be increased.

SLEEP LOSS AND EPILEPTIFORM DISCHARGES

Total sleep deprivation initially increases cerebral irritability, which may result in epileptiform discharges in predisposed individuals.^{3,16,22,27-29,36-38,41,71-76,87,104,177,184,201,236,248,267-269,318}

Because of this, sleep deprivation has been used to provoke abnormal paroxysmal electroencephalographic discharges in individuals with suspected epilepsy.⁸⁷ One night of total sleep loss is combined with other techniques of activation in clinical practice.²⁰¹ However, increased irritability appears to be limited to the first 2 days of total sleep deprivation; after that, extreme sleepiness reduces cerebral electrical excitability.

Because total sleep deprivation of 2 days or less under clinical laboratory conditions does not induce epileptiform discharges in normal healthy individuals, false positives rarely occur.^{28,29,202,318} Only one child (8%) of a group of 12 normal children showed an abnormal electroencephalogram after a short period of total sleep deprivation.¹⁰⁴

However, prolonged total sleep deprivation combined with other stressors may induce abnormal cerebral discharges in healthy individuals.^{3,111} On continuous recordings of brain waves over 90 hours, a third of healthy subjects exhibited paroxysmal activity lasting for only a few seconds at a time. One subject showed, however, a total of 2.5 hours of spike-and-wave activity in one day. None of the subjects experienced grand mal seizures, but some exhibited “absence” or psychomotor seizures. Especially for the individuals with a pre-existing susceptibility, sleep deprivation sets the stage for epileptic seizures resembling short periods of inattention and battle shock.¹¹¹

Briefly, all of us could develop psychomotor-type epileptiform discharges under the combined influence of sleep loss and other stressors. Some individuals are more susceptible than others.

SLEEP LOSS AND PHYSICAL WORKING CAPACITY

Maximal oxygen consumption is a measure of cardiovascular fitness or overall aerobic work capacity. Oxygen consumption increases with increasing physical workload. As physical workload continues to increase, we eventually reach a point where the pulmonary/cardiovascular system becomes incapable of supplying additional oxygen to the working skeleton and muscles, and oxygen consumption plateaus despite increasing physical workload. This plateau represents the maximal rate of oxygen consumption—that is, maximal aerobic capacity, $\text{VO}_2 \text{ max}$.³³⁴ A psychological factor of willingness to endure acute discomfort enters into a $\text{VO}_2 \text{ max}$ testing because the test is terminated by subjects. Aerobic working capacity can also be measured indirectly by the increase in heart rate and the speed of return to resting heart rate following standardized physical work regimens, such as the Harvard Step Test.^{52,66}

In 1970, Vogel and Glaser studied three male subjects who underwent maximal and submaximal working capacity tests on a bicycle ergometer before and after sleep deprivation. Reviewing their data, Harris and O'Hanlon

reported that after 72 hours of total sleep deprivation, the VO_2 max values of the three subjects were reduced by 3.2%, 6.0%, and 3.8% against the baseline.¹¹⁰ Plyley et al. observed a 6.9% decrease of VO_2 max during 64 hours of sleep deprivation.²³³ Martin and Chen¹⁷⁵ reported a decline in physical performance after 50 hours of sleep deprivation. The endurance-run time to exhaustion was reduced by 20% among the sleep-deprived. Takeuchi et al.²⁸⁴ found that vertical jump performance decreased after 64 hours of sleep deprivation. Yeager et al., however, observed that 45 hours of sleep deprivation did not change maximal aerobic capacity.³³⁴ Martin showed no change in VO_2 max after 30 hours of sleep deprivation.¹⁷³ Symons et al. found that sleep loss of up to 60 hours did not impair the capability for physical work.²⁸³

Pickett and Morris²³¹ found that cardiovascular endurance was not affected by total sleep deprivation of 30 hours, but it was affected by food and water deprivation of the same duration. Brodan and Kuhn,⁵² using the Harvard Step Test, found that young men showed about a 5% drop in cardiovascular fitness during the first 48 hours of total sleep deprivation. Their cardiovascular fitness began to recover, however, and even increased, after continued sleep deprivation; after 5 days of total sleep loss, the mean score exceeded the baseline mean by 5%. The most surprising finding was a sharp drop of nearly 15% in cardiovascular fitness on the first day after the recovery sleep. In much younger subjects (ninth-graders), Copes and Rosentsweig⁶⁶ found a decline of cardiovascular fitness as measured by the Harvard Step Test during total sleep loss.

Orlee et al. reported that men lost their top physical conditioning quickly after one night of total sleep deprivation.²¹⁶ For physically conditioned men, however, the loss was limited to fitness gained by hard training. The degradation brought the fitness level down to the pretraining baseline but not below.

Total sleep deprivation of 24–30 hours slowed reaction time as well as speed of movement.^{56,231} Resting electromyographic activity was reported to be reduced during total sleep deprivation.¹¹⁶ Summarizing the results of past studies, Wilkinson commented, however, that electromyographic changes are unrelated to hours of sleep loss.³²⁴

It has been well established that continuous muscular activity, such as walking, can help sleep-deprived subjects remain awake.¹³⁸ Naitoh et al. observed that all subjects kept themselves physically active to stay awake; for example, a subject was willing to keep moving on his feet, walking 8.3 times more during the 165–191 hours of total sleep deprivation, compared with the 26-hour period at the start of the study.

Briefly, physical work capacity appears not to show major deterioration as a result of total sleep deprivation of 3 days or less. Movement speed, however, is slowed down. Willingness and ability to remain physically active (e.g., by walking) are severely tested by the increasing desire to rest.

ANTIDEPRESSIVE EFFECTS OF SLEEP LOSS

Health effects of sleep deprivation are not always negative. The antidepressant effects of total sleep deprivation have been well established. This is an area that is still actively researched. The bibliography of this chapter cites more than 30 references on it. Total sleep deprivation provides temporary relief from depression in one-third to one-half of endogenously depressed patients, but it is less effective in patients with involutional depression. With respect to the other major category of depression, reactively depressed patients benefit from sleep loss more if they

have more somatic complaints (such as disturbed sleep and poor appetite) and large diurnal fluctuation in moods, as compared with few somatic complaints and poor circadian rhythm. Typically, a single night of total sleep deprivation is repeated over several weeks until the desired amelioration of depression is achieved. The patients must remain awake between 0400 and 0600 to get full antidepressant benefit from sleep deprivation. Cole and Muller⁶³ reported that when elderly depressives (57–79 years old, average age 69) were given repeated (once or twice a week) 36-hour periods of total sleep deprivation therapy, 9 (60%) of 15 patients responded to the therapy and 6 (40%) had a good outcome. However, total sleep deprivation therapy may trigger a manic phase.^{316,317}

Post et al.²³⁵ sampled lumbar cerebrospinal fluid from depressive patients to study central amine metabolism as reflected by levels of 5-hydroxyindoleacetic acid (5-HIAA), homovanillic acid, and 3-methoxy-4-hydroxyphenylglycol. Total sleep deprivation changed the central amine metabolism of the depressed patients, causing a decrease in 3-methoxy-4-hydroxyphenylglycol. The other parameters increased. In a study by Livrea et al.,¹⁶³ lumbar cerebrospinal fluid was examined for homovanillic acid and 5-HIAA before and after total or REM sleep deprivation. Cerebrospinal fluid levels of homovanillic acid and 5-HIAA were not affected by 30 hours of total sleep deprivation, but 5-HIAA increased after 2 nights of REM sleep deprivation.

Two hypotheses attempting to explain the antidepressant effects of total sleep deprivation are:

- (1) total sleep deprivation assists in resynchronization of disordered circadian rhythms and re-entrainment to the 24-hour societal rhythm
- (2) total sleep deprivation lowers an abnormally high arousal level in depressives.

REM sleep deprivation also has antidepressant effects.^{304,305} The REM sleep deprivation procedure consists of awakening subjects every time they go into REM sleep. This is continued for six nights or until 30 awakenings per night are reached (REM frequency increases as deprivation accumulates), whichever comes first. Subsequently patients are permitted a single night of uninterrupted sleep. The REM sleep deprivation procedure is repeated until the desired amelioration of depressive symptoms is obtained.

In brief, total or REM sleep deprivation helps to temporarily reduce depression in some depressive patients. Mood effects of total or REM sleep deprivation in normal individuals are discussed in the following section.

SLEEP LOSS AND QUALITY OF LIFE

The most serious health cost in its broadest sense is a lowered quality of life during sleep deprivation. Sleep loss results in chronic excessive fatigue and sleepiness, sagging motivation for work, and poor job performance leading to frustrations and conflicts with other workers. The quality of life will be discussed in terms of (1) mood and motivation to work, (2) excessive daytime sleepiness and fatigue, and (3) mental health.

Mood and Motivation to Work

In the *Handbook on Human Engineering Data* (second edition) published by Tufts College for the Office of Naval Research in 1952, 17 papers on sleep deprivation are reviewed. The editors were surprised to see that "there are no significant physiological changes with up to 200 hours of sleeplessness" and that

"subjective attitude (appearance, mood and behavior) is the only factor severely affected by sleep reduction." This conclusion is still valid.^{116,118,119}

One night of total sleep deprivation was found to influence six factors: sleep/wakefulness, stress, euphoria, energy, irritation, and concentration, in a complex, but highly predictable, manner. For example, one night of total sleep deprivation lowered wakefulness and energy ratings, but did not significantly change stress and euphoria.⁴⁴ Simple negative mood changes, such as feeling tired, are consistently reported after total sleep deprivation and can be used to gauge the extent of accumulated sleep debt. Subjects felt progressively more negative and less positive during total sleep deprivation, and these mood changes showed strong circadian rhythm.^{199,200} Thus, unlike depressives, normal subjects do not experience large positive mood changes or feelings of well-being after sleep deprivation.^{44,69}

In the first scientific study of partial sleep deprivation, Mary Smith studied herself. She shortened the usual period of sleep over three consecutive nights by 1.5, 3.5, and 5.5 hours.²⁷³ She experienced a double feeling tone—unpleasant muscular weariness that became pain at times, and pleasant sensations of exhalation and power. For the most part, the pleasant aspect was dominant. Johnson and MacLeod¹²⁵ reduced the sleep of two subjects by 30 minutes, every two weeks, from their customary 7.5 hours to a minimum of 4 hours per 24 hours. Using the Profile of Mood States, they found that the subjects were less "happy," less "friendly," more "fatigued," and increasingly irritable. The subjects experienced difficulties maintaining concentration when the sleep period was reduced to 5.5 hours or less.

In another gradual sleep reduction study,¹⁰⁰ two young couples reduced their sleep by 30 minutes every two weeks until total sleep time reached 6.5 hours. They continued to reduce sleep at a rate of 30 minutes every three weeks. When total sleep time was down to 5 hours, the rate of sleep reduction became 30 minutes every four weeks to give the subjects more opportunity to adapt to the shorter sleep and longer day. Eventually, the subjects felt that they found the minimum sleep they needed, the point where their sleep was maximally reduced without jeopardizing their jobs and schoolwork. Over a 7-month period, one couple reduced their sleep time from 8 hours to 5 hours. The other couple reduced their sleep from 8 hours to 4.5 hours over an 8-month period. Both couples slept for a month at these low levels. Subsequently, the sleep period was lengthened by 30 minutes for a 2-week period, after which they were allowed ad lib sleep regimens.

The couples reported that they decided to stop reducing their sleep because they were overwhelmingly tired, they were falling asleep in class, playing cards, or visiting friends, and they had difficulty remaining alert while driving. However, objective school and job performances did not suffer during the partial sleep deprivation.

Webb and Agnew³¹⁵ examined 15 subjects who reduced sleep to 5.5 hours and maintained that amount for 60 days. The moods of these subjects showed initial dips but generally returned to baseline as partial sleep deprivation continued. During the study period, the subjects showed performance degradation that appeared to be due to boredom and lowered motivation.

In brief, mood deteriorates and motivation to work hard is lowered during total and partial sleep deprivation. Although controlled studies of regular gradual reduction in nightly sleep have demonstrated that we have a potential to

adjust to partial sleep deprivation, these results are not directly applicable to the shiftworker. In shiftwork, partial sleep deprivation occurs acutely when nightshift work begins and, unlike strictly controlled studies, the amount of sleep loss may vary from day to day. Greater experience on a shiftwork schedule has not been shown to be associated with reduced complaints about sleep loss.

Excessive Daytime Sleepiness and Fatigue

Naitoh¹⁹⁹ reported that the levels of fatigue and sleepiness increase and decrease in a circadian manner and that total sleep deprivation of 2 nights increased subjectively rated fatigue and sleepiness without destroying these circadian rhythms. Sleepiness, as measured by the Stanford Sleepiness Scale,¹¹⁴ peaks around 0200–0600 of the first night of total sleep deprivation. Once subjects pass this critically sleepy period, they feel much less sleepy even though they remain awake. However, Carskadon and Dement⁵⁸ found that objective sleepiness, as measured by the Multiple Sleep Latency Test, lost its normal circadian rhythm during the first night of total sleep deprivation; sleepiness peaked around 0600 the next morning and remained at peak level throughout the 2 nights of total sleep deprivation.

As shown in the studies of Friedman et al.¹⁰⁰ and Johnson and MacLeod¹²⁵ discussed in the preceding section, subjective feelings of tiredness and sleepiness provide an early warning of excessive sleep debt. Impairment of job performance appears much later than daytime feelings of excessive tiredness and sleepiness. In real workplace situations, worker motivation is an important variable with respect to how closely performance decrements follow sleep loss.

In brief, increased feelings of tiredness and sleepiness reliably follow total or partial sleep deprivation, reducing quality of life. These feelings constitute an early warning that serious deterioration in job performance will follow unless more sleep is obtained.

Mental Health

As mentioned previously, the most obvious and consistent changes due to total and partial sleep deprivation are psychological. When investigators lived with sleep-deprived subjects, they often observed frequent, but transient, psychotic behavior.³² These behavioral pathologies are easily missed because of their transience. Whether a subject shows transient psychopathology during total sleep deprivation depends on age, physical health, psychological stability, and the environment of the study.

Total sleep deprivation experiments represent a complicated social psychological arrangement.^{191–193} An illustration of the impact of experimental environments is found in the differences between the results of Tyler's study^{293–295} and those from the Walter Reed Army Medical Institute of Research.^{192,327}

Tyler's study involved 350 volunteers under military discipline during the period of 1942–1946. Under the stringent, stressful military exercise environment, 112 hours of total sleep deprivation caused more than 70% of the subjects to complain of auditory and visual illusions. Seventy-six of these men dropped out before the conclusion of the study for a variety of psychosomatic complaints. Seven men had to be removed from the study because they developed hallucinations and bizarre "psychotic" behaviors. The high attrition occurred despite excellent morale at the start and a considerable incentive offered for completing the study.

The Walter Reed study was conducted in a laboratory environment. The staff maintained a friendly and egalitarian atmosphere in order to keep frustration and aggression at a minimum. Gentle methods such as walking, playing games, holding conversations, and encouragement from staff were used to help 74 soldiers stay awake for 72-98 hours. No subjects dropped out, and no "psychotic" breakdowns were observed although visual hallucinations were reported.

Thus, the sociology of total sleep deprivation or the psychological characteristics of the environment play a critical role in determining mental health during total sleep loss.

Prior mental stability is also a determinant of a subject's psychological responses to total sleep deprivation.^{134,167,168} Pasnau et al. reported a study involving 205 hours of total sleep deprivation.²²⁴ One of the volunteer subjects experienced a panic response and all subjects had psychological problems, but they found no evidence of psychosis. In 1968, an editorial in the *Journal of the American Medical Association*²⁷² stated, on the basis of data later published by Kollar et al.¹⁴² and Pasnau et al.,²²⁴ that sleep deprivation does not cause mentally healthy people to become psychotic. Dement⁷⁹ similarly pointed out that REM sleep deprivation does not lead to psychosis. REM sleep deprivation does not cause intensification of thought disturbances, perceptual and motor disorganization, or increased withdrawal.^{301,305,306}

In brief, total sleep deprivation does not cause permanent psychosis. Bizarre visual illusions, hallucinations, paranoid mentations, and other behavioral pathologies may be seen, but they are limited to the period of sleep deprivation and disappear after recovery sleep. Hostile or stressful work environments are more prone to produce abnormal responses than friendly supportive environments.

DISCUSSION AND SUMMARY

On the whole, the health consequences of total, partial, or selective sleep deprivation appear to be much smaller than might have been anticipated from the overwhelming sense of sleepiness, tiredness, and sluggishness it can cause. We can conclude that the only substantial and potentially serious effect of sleep deprivation is a reduction in the quality of life as defined by a person's feeling of well-being, willingness to work hard, and feeling of being efficient, wide awake, fresh, and in control. This does not mean that sleep deprivation fails to cause small changes in human biochemistry and physiology.

The belief that sleep should be 7-8 hours long, should offer a refreshed feeling upon awakening, and is needed for physical and mental recuperation appears to have resulted in unwarranted anxiety about sleep loss. This anxiety can affect how a person interprets minor, but perceptible, changes during sleep loss, such as tiredness, sleepiness, lapses of attention, inability to concentrate, and an overall feeling of not being well. With anxiety, these minor psychological changes may be interpreted as representing serious mental harm. The emotional reaction following such an interpretation can cause a person to urgently seek sleep in hopes of avoiding further harm, even to resort to the use of ethanol, sedatives, tranquilizers, and hypnotics.

Schachter²⁶¹ and Schachter and Singer²⁶² have proposed that the nature of emotional response is determined by two components: some perceptible physiological changes and the individual's appraisal of these physiological changes. For example, an increase in heart rate and facial flushing after drinking alcoholic beverages may be implicitly interpreted as a warm satisfying alcohol effect by a

habitual drinker, but as a dangerous or uncomfortable effect by someone who rarely drinks.

Carskadon et al.⁶⁰ reported that a group of 109 chronic insomniacs actually differed very little, in terms of total sleep time and sleep latency, from a group of 87 normal sleepers. They did differ in the number of awakenings during sleep. The chronic insomniacs may have physiological or biochemical problems that cause their sleep to be fragmented. It could be argued that, since these insomniacs have normal total sleep time, they may only be suffering psychologically from the awakenings because they interpret them as life or health threatening. Their chronic fear of getting nothing but poor sleep may cause them to suffer much more than a normal sleeper would from a nocturnal awakening. Perhaps an overlay of fear can aggravate what is basically a physiological variation on the norm into a significant psychological problem.

How has the popular belief that poor sleep is dangerous to health come about? Anxiety about the effects of poor sleep or total lack of sleep may have an origin in experiments conducted near the turn of the century and reported by Pieron in 1913²³² and later by Kleitman.¹³⁸ They reported physical harm and even death among animals that had been subjected to total sleep deprivation. We have shown that, at least in humans, total sleep deprivation of up to 205 hours does not pose serious health problems.^{130,141,142,202,203,224,252} Similarly, chronic reduction of sleep time does not produce any physical harm.^{100,125,315}

In addition to supposedly producing physical harm, sleep deprivation is also believed to result in mental harm, i.e., psychosis or intensification of psychopathology.³¹⁹ The belief that psychosis of sleep deprivation occurs in normal individuals developed many years ago and is based on dramatic examples reported by Katz and Landis¹³³ and others. Katz and Landis described a 24-year-old man who was convinced that sleep was a habit and could be broken without any ill effects. He remained awake for 231 hours before developing delusions of persecution, at which time the study was terminated. In another study, a large number of young soldiers, marines, and civilians underwent paratrooper-like training that included a 35-mile night march; some subjects suffered a transient psychosis with paranoid mentation.^{293,294}

Careful evaluation of these and other studies shows that psychosis was not caused by sleep deprivation itself, but by a combination of sleep loss with other stressors. The previously mentioned 1968 editorial in the *Journal of the American Medical Association* made a clear effort to correct the view that sleep deprivation causes mental harm. The editorial stated that sleep loss would not produce psychopathological reactions extending beyond the period of sleep deprivation and that "patients who suffer from periods of insomnia can be reassured as to the transiency and safety of a brief sleepless period"; it also said that no medication is necessary to protect patients against the psychosis of sleeplessness. The editorial cited the studies that found total sleep deprivation to be beneficial for temporarily relieving depression in some depressive patients.

In the 1960s and 1970s, REM sleep deprivation was also thought to cause mental harm.^{61,79,88,119,160} However, it has since been shown to provide safe and effective, although temporary, relief from endogenous depression.

Thus, fear that total sleep and REM sleep deprivation directly cause physical and mental harm is groundless.

This report has attempted to provide information about health consequences of total sleep deprivation. We are surprised to learn from the surveyed literature

that sleep deprivation produces only very small biomedical effects. However, some caveats are necessary.

For workers needing maximum alertness and uninterrupted concentration, such as air traffic controllers, heavy equipment operators, power plant operators, and blood bank technicians, anxiety about the effects of chronic partial sleep deprivation is warranted, particularly insofar as it may cause lapses of attention and inability to concentrate. Many physiological changes have the potential to cause major catastrophes. These workers' appropriate anxiety about their sleep loss may increase the likelihood of errors and may also produce health complaints associated with chronic anxiety.

Almost all of the past and current research on sleep deprivation is based on highly controlled laboratory studies using short-term data collection. Such studies are not able to assess the complex patterns of sleep deprivation combined with various stressors seen in working environments. Thus, the surveyed literature may be biased by protocols designed more to be simple, clean, and easy to interpret than to answer questions about the biomedical consequences of sleep loss in real life circumstances. Hence, the surveyed literature may have underestimated the true biomedical impact of sleep loss.

For example, most research reports are based on responses to a single exposure to sleep deprivation. Since real life experience more often involves repeated exposures to sleep loss, the findings in the literature may not be directly applicable. Health problems in shiftworkers, who are more apt than other workers to endure chronic sleep deprivation, have been extensively investigated (see Chapter 7). Gastrointestinal disorders, cardiovascular disease, and numerous other medical conditions occur more frequently or are aggravated in this group. These effects may be due wholly to disruption of biological rhythms, but the possibility that chronic sleep deprivation contributes to them cannot be dismissed.

Another caveat is that the findings of these studies cannot be generalized to the middle-aged or older population, especially not to people with less than ideal physical and mental fitness. Most of the studies have been conducted on young, physically and mentally fit people, usually students at universities. Worst of all, only a few (e.g., a series of fascinating studies on 5-day military training courses by Opstad, Palmblad, and others at the Norwegian Defense Research Establishment^{1,2,209-215,219-222,249-251}) measured the interaction of physical and psychological stressors with sleeplessness. Since sleeplessness in daily experience often occurs concurrently with job-related, and other, stressors, results of these single-factor studies cannot be generalized to determine health consequences of sleep deprivation in daily life. If combining sleep loss with various stressors is still found to lead to no lasting physical or mental harm, it must be kept in mind that even a transient psychotic episode can be detrimental to health if it happens during dangerous military or industrial activity.

It has been said in jest that all sleep deprivation does is make us sleepy. However, sleepiness is a mystery of life worth careful investigation. Understanding it would help us gain a full appreciation of the nature of sleep and the impact of sleep loss on our bodies.

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